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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,832	01/03/2006	Susan M. Freier	RTS-0428USA	2330

71476 7590 01/02/2009

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EXAMINER	
MCGARRY, SEAN	

ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
01/02/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/511,832	FREIER, SUSAN M.	
	Examiner	Art Unit	
	Sean R. McGarry	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 4-24* is/are pending in the application.

4a) Of the above claim(s) *15-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 4-14, 21-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Official Action is in response to the papers filed 10/01/08. Applicant provides no arguments in response to the rejections of record, but assert only that the amendment to claim 1 overcomes all of the rejections. The amendment to claim 1 is addressed in the rejections below. It is noted that there is no amendment to claim 11 nor is there any indication why it should not be rejected as in the previous Official Action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10, 12-14, and 21-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 21 has been amended to recite ”inhibits. . . by at least 51%”. The amendment presents ambiguity into the claimed invention. One in the art would be hindered in being apprised of the metes and bounds of the invention since there is no context for the percent inhibition required. One in the art may have a compound that inhibits by 51% under one condition and perhaps by 20% under another. It is further noted that the 11βHSD1 that is reduced by 51% is not required to be the 11βHSD1 of SEQ ID NO: 3. The remaining claims are rejected in so far as they depend from claim 1.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4, 5, and 11 rejected under 35 U.S.C. 102(b) as being anticipated by Hatakeyama et al [Front. Sci. Ser. Vol. 29 :173-174, 2000 , cited by applicant on form 1449, filed 4/19/02].

Hatakeyama et al disclose 24mer phosphorothioate antisense oligonucleotides complementary to the 5' region of 11β-Hydroxysteroid Dehydrogenase [11β-HSD] mRNA isoforms 1 and 2 containing their respective start codons. It is noted that the antisense are targeted to human sequence [SEQ ID NO: 3 of the instant invention is the human sequence] and fuerthermore it is shown that the activity of 11β-Hydroxysteroid Dehydrogenase 1 was reduced by 60%. It is noted that 60% reduction of activity does not necessarily correspond to at least 51% inhibition of expression, but applicant is also directed to the rejection under 35 U.S.C. 112, second paragraph above.

Claim 11 is rejected under 35 U.S.C. 102(a) as being anticipated by Souness et al [Steroids Vol. 67 (3-4):195-201, 2002, cited by applicant on form 1449, filed 4/19/02].

Souness et al disclose a phosphorothioate antisense oligomer targeted to a 20 bp sequence spanning the ribosome binding/translation initiation start site of 11β-HSD1 (see page 196, column 1 bottom of page, for example). It is disclosed that the oligonucleotides were included in a composition of oligonucleotide and sterile water at page 196, for example (see column 2, top of page).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 4-14, and 21-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Souness et al., Hatakeyama et al., Bennett et al. [US 5,998,148], and Baracchini et al. [5,801,154].

The claimed invention is drawn to antisense oligomers targeted to specified regions of 11βHSD 1 that are 8-80 nucleobases in length that may contain various specified/recited modifications and compositions comprising such oligomers.

Souness et al has taught phosphorothioate antisense targeting the 5' region containing the start codon of 11βHSD1 mRNA. Souness used antisense strategy to examine biological properties of 11βHSD1 as well as 11βHSD2. The Disclosure of Souness et al shows the importance of 11βHSD1 in vascular contraction. It is asserted at page 200 that further antisense experiments will be performed to make further determination of other biological functions/properties of 11βHSD1.

Hatakeyama et al used phosphorothioate antisense oligonucleotides targeted to the 5' region of 11βHSD1 containing the start codon to determine the function of 11βHSD1 in vasculature and assert that 11βHSD1 has function in regulating blood pressure and vascular tone. Hatakeyama et al have targeted human 11βHSD1.

The prior art above does not specifically disclose the recited SEQ ID NO:3 or specific modifications or composition constituents recited in the claims or specifically

inhibiting by 51%. The prior art cited below, however shows that these recited limitations were well known and routinely used in the art at the time of the instant invention.

Bennett et al have taught general targeting guidelines at columns 3-4, for example. It has been taught to target 5'untranslated regions, start codons, coding regions, and 3'untranslated regions of a desired target, for example. It has been taught in column 5, for example, that antisense compounds are commonly used as research reagents and diagnostics, for example. At column 5 it has been taught that antisense oligonucleotides 8-30 nucleotides in length are particularly preferred. At columns 6-7 it has been taught preferred antisense oligonucleotides contain modified internucleoside linkages including phosphorothioate linkages, for example. At columns 7-8 it has been taught that preferred antisense oligonucleotides comprise modified sugar moieties including2'-O-methoxyethyl. It has also been taught to modify nucleobases in antisense oligonucleotides at column 8-9 which includes the teaching of 5-methyl cytosine and at column 10 it has been taught chimeric antisense oligonucleotides. All of the above referred to modification are known in the art to provide beneficial attributes to antisense oligonucleotides such as increased hybridization and nuclease protection, for example. At columns 10-24, for example it has been taught numerous "carriers" for antisense oligonucleotides. In table I it has been taught the successful targeting of those regions taught in columns 3-4 with chimeric phosphorothioate oligonucleotides having 2'-MOE (a 2'-O-methoxyethyl modification).

Baracchini et al have taught, at column6 for example, that antisense oligonucleotides can be used for research purposes and have also taught at column 6

that antisense oligonucleotides can be modified in their sugars, backbone linkages and nucleobases and that such modifications are desirable in antisense since these modifications have desirable properties such as, for example, enhanced cellular uptake, enhanced affinity for nucleic acid targets and increases stability in the presence of nucleases. Baracchini et al provide specific examples of such modifications at columns 6-8 and in Example 1, for example. These specific examples taught by Baracchini et al include phosphorothioate linkages, 2'-O-methoxyethyl sugars, 5-methylcytosine and chimeric oligonucleotides, for example. Tables 1-4 show the successful design and use of modified oligonucleotides in cells in culture, for example. Table I therefore reflects the successful practice of general antisense design taught at columns 8-10, for example. At column 4 it has been taught various carriers for antisense delivery. It has been taught at column 8 that antisense are preferably 8 to 30 nucleotides and that it is more preferable to make antisense oligonucleotides that are 12 to 25 nucleotides in length, for example.

It is noted that looking at the tables provided in Baracchini and Bennett et al that it is not unexpected to obtain antisense compounds that inhibit by at least 51% and it is readily apparent from those documents that such compounds can be routinely screened for.

Based on the teachings of the prior art as a whole it is clear that it would be obvious to make modified antisense oligonucleotides as claimed in the instant claims since the prior art has specifically shown the making of specific modified antisense to 11βHSD1 asserted that more antisense experimentation of 11βHSD is desirable and the prior art has also shown to target the recited regions of a target gene and also to

use the specific and recited modifications for the benefits as taught in the art references, for example. The art has shown that there is a motivation to make antisense to 11βHSD1 and has also shown that the specified target regions were routinely shown in the art to be desirable target regions and that the specified modification and formulation are all desirable for various reasons in the application of antisense technology. The prior art has also clearly shown that one in the art would have at the very least a reasonable expectation in making the claimed invention. The references do not specifically disclose SEQ ID NO:3 as a target nucleic acid. However SEQ ID NO: 3 was known in the art at the time of applicant invention and is a human11βHSD1 sequence. It is clear that the intention of scientific discovery is to improve the human condition and perhaps make pharmaceutical compounds to make a profit. With that in mind it is clear that targeting a human sequence is clearly an obvious choice as the prior has indeed already targeted a human 11βHSD1 via antisense compounds.

The invention as a whole would therefor have been *prima facie* obvious to one in the art at the time the invention was made.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean R. McGarry whose telephone number is (571) 272-0761. The examiner can normally be reached on M-Th (6:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, J. Douglas Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Primary Examiner
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